

What is claimed is:

1. An isolated nucleic acid encoding human neutral sphingomyelinase.
2. The nucleic acid of claim 1 where the nucleic acid comprises the sequence of SEQ ID NO:1, or the complement thereto.
3. The nucleic acid of claim 1 where the nucleic acid codes for the human neutral sphingomyelinase of SEQ ID NO:2.
4. The nucleic acid of claim 1 where the human neutral sphingomyelinase has a molecular weight of about 44 kDa as determined by polyacrylamide gel electrophoresis using sodium laurylsarcocine.
5. The nucleic acid of claim 1 where the nucleic acid has at least about 80 percent sequence identity to SEQ ID NO:1, or the complement thereto.
6. The nucleic acid of claim 1 wherein the polynucleotide is cDNA.
7. The nucleic acid of claim 1 wherein the polynucleotide is RNA.
8. A recombinant vector comprising the nucleic acid of claim 1.
9. A host cell comprising the vector of claim 8.
10. A method of producing human neutral sphingomyelinase comprising culturing a host cell of claim 9 under conditions suitable for expression of human neutral sphingomyelinase.

11. A nucleic acid that hybridizes to the sequence of SEQ ID NO:1 under normal stringency conditions.

12. The nucleic acid of claim 11 where the nucleic acid hybridizes to the sequence of SEQ ID NO:1 under high stringency conditions.

Sub B2 13. A method of identifying a compound useful in the diagnosis or treatment of a human neutral sphingomyelinase related disorder, comprising contacting a candidate pharmacological agent with human neutral sphingomyelinase or fragment or derivative thereof and analyzing the mixture of the candidate agent and human neutral sphingomyelinase or fragment or derivative thereof.

14. The method of claim 13 wherein the human neutral sphingomyelinase has a sequence represented by SEQ ID NO:2.

15. The method of claim 13 wherein

- 1) a mixture is formed of i) a human neutral sphingomyelinase cleavage target, ii) the human neutral sphingomyelinase or fragment or derivative thereof, and iii) a candidate pharmacological agent;
- 2) the mixture is treated under conditions whereby, but for the presence of the candidate agent, the human neutral sphingomyelinase or fragment or derivative cleaves the cleavage target to yield a cleavage product; and
- 3) the presence of the cleavage product is detected, wherein a reduced concentration of the cleavage product relative to a control mixture that does not contain the candidate agent identifies the candidate agent as a compound potentially useful in the diagnosis or treatment of a human neutral sphingomyelinase related disorder.

16. The method of claim 15 wherein the human neutral sphingomyelinase cleavage target is sphingomyelin.

17. The method of claim 15 wherein the human neutral sphingomyelinase cleavage product is ceramide.

18. An isolated human neutral sphingomyelinase having an apparent molecular weight of about 44 kDa as determined by polyacrylamide gel electrophoresis using sodium laurylsarocene.

19. An isolated human neutral sphingomyelinase of claim 18 comprising a sequence represented by SEQ ID NO:2.

20. An isolated polypeptide having at least about 70 percent sequence identity to SEQ ID NO:2.

21. A method for modulating N-SMase activity comprising administering to human cells a modulation effective amount of a nucleic acid of claim 1 or fragment or derivative thereof.

22. A method for modulating N-SMase activity comprising administering to human cells a modulation effective amount of an isolated human neutral sphingomyelinase of claim 18 or fragment or derivative thereof.

23. A method for treating a disorder associated with N-SMase comprising administering to a patient suffering from or susceptible to such disorder an effective amount of an isolated nucleic acid of claim 1 or fragment or derivative thereof.

24. The method of claim 23 wherein the disorder is an inflammatory disorder, arthritis, osteroarthritis, Crohn's disease, obesity, diabetes, cirrhosis, susceptible tumors, central nervous system disorder, vascular restonsis, arterial occlusion arising from plaque formation, cardiac disease where LV dysfunction

occurs, hypercholesterolemia, cholesteryl ester storage disorder, renal failure, HIV infection, depression, schizophrenia, neurodegeneration and Alzheimer's disease.

25. A method for treating a disorder associated with N-SMase comprising administering to a patient suffering from or susceptible to such disorder an effective amount of an isolated human neutral sphingomyelinase of claim 18 or fragment or derivative thereof.

26. The method of claim 25 wherein the disorder is an inflammatory disorder, arthritis, osteroarthritis, Crohn's disease, obesity, diabetes, cirrhosis, susceptible tumors, central nervous system disorder, vascular restonsis, arterial occlusion arising from plaque formation, cardiac disease where LV dysfunction occurs, hyperchloesteroloemia, cholesteryl ester storage disorder, renal failure, HIV infection, depression, schizophrenia, neurodegeneration and Alzheimer's disease.

27. A method of maintaining samples of sperm or seminal fluid comprising providing a mixture comprising sperm or seminal fluid and an effective amount of an a fragment or derivative of human neutral sphingomyelinase.

• 28. The method of claim 27 wherein the mixture comprises human sperm or seminal fluid.

29. A storage sample of sperm or seminal fluid comprising sperm or seminal fluid and a storage effective amount of a fragment or derivative of human neutral sphingomyelinase of claim 18.

30. A method to reduce TNF- α induced apoptosis of mammalian cells comprising administering to a mammal an effective amount of antibody against N-SMase or fragment or derivative thereof.